

Figure 3 illustrates changes in LVDP during normal perfusion with Krebs buffer in the presence (10-15 min) and absence (15-20 min) of MnDPDP.

Figures 4 (A) and 4 (B) show clearance of  $\Delta R_1$  from blood and infarcted myocardium.

Figure 4 (C) shows the increase in  $\Delta R_1$  in normal myocardium.

Figures 5 (A) and 5 (B) show plots of  $\Delta R_1$  ratio increase with time for normal myocardium.

Figure 6 shows the difference in  $R_1$  values between normal and reperfused infarcted myocardium.

**IN THE CLAIMS:**

Please cancel claims 1-16 without prejudice or disclaimer and add the following new claims to the application.

31(New). A method of detecting myocardial ischemia in a human or non-human body, said method comprising administering to said body a physiologically acceptable manganese complex or salt thereof at a dosage of 0.001 to 0.2 mmol/kg bodyweight, subjecting said body to a magnetic resonance imaging procedure capable of generating images with time intervals of less than 0.5 seconds and thereafter providing a series of images of the myocardium of said body and identifying regions of abnormal blood flow.

32(New). A method as claimed in claim 31 wherein said magnetic resonance imaging procedure is one capable of generating images with time intervals of less than 100 milliseconds.

33(New). A method as claimed in claim 31 wherein said imaging procedure is a gradient echo or echo planar imaging procedure.

34(New). A method as claimed in claim 33 wherein said imaging procedure is an inversion recovery echo planar imaging procedure.

35(New). A method as claimed in claim 33 wherein said imaging procedure is one in which TI (inversion time) is 100 to 800 msecs, TR (repetition time) is 2000 msecs and TE (echo time) is less than 20 msecs.

36(New). A method as claimed in claim 31 wherein said manganese complex or salt thereof is administered at a dosage of 0.005 to 0.2 mmol/kg bodyweight.

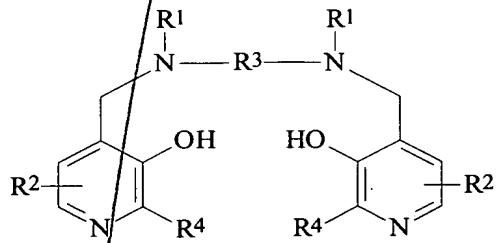
37(New). A method as claimed in claim 36 wherein said manganese complex or salt thereof is administered at a dosage of 0.01 to 0.05 mmol/kg bodyweight.

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38(New). A method as claimed in claim 31 wherein said manganese complex is a manganese chelate complex having a  $K_a$  value of from  $10^7$  to  $10^{25}$ .

39(New). A method as claimed in claim 38 wherein said chelate has a  $K_a$  in the range of from  $10^{12}$  to  $10^{22}$ .

40(New). A method as claimed in claim 38 wherein said chelate has a  $K_a$  value smaller by a factor of at least  $10^3$  than the  $K_a$  value of a corresponding ferric ( $Fe^{3+}$ ) chelate.

41(New). A method as claimed in claim 38 wherein said manganese chelate comprises a chelating compound of formula I:



(I)

or a salt thereof

wherein in formula I

each R<sup>1</sup> independently represents hydrogen or -CH<sub>2</sub>COR<sup>5</sup>;

R<sup>5</sup> represents hydroxy, optionally hydroxylated alkoxy, amino or alkylamido;

each  $R^2$  independently represents a group  $XYR^6$ ;

$X$  represents a bond, or a  $C_{1-3}$  alkylene or oxoalkylene group optionally substituted by a group  $R^7$ ;

$Y$  represents a bond, an oxygen atom or a group  $NR^6$ ;

$R^6$  is a hydrogen atom, a group  $COOR^8$ , an alkyl, alkenyl, cycloalkyl, aryl or aralkyl group optionally substituted by one or more groups selected from  $COOR^8$ ,  $CONR^8_2$ ,  $NR^8_2$ ,  $OR^8$ ,  $=NR^8$ ,  $=O$ ,  $OP(O)(OR^8)R^7$  and  $OSO_3M$ ;  $R^7$  is hydroxy, an optionally hydroxylated, optionally alkoxylated alkyl or aminoalkyl group;

$R^8$  is a hydrogen atom or an optionally hydroxylated, optionally alkoxylated alkyl group;

$M$  is a hydrogen atom or one equivalent of a physiologically tolerable cation;

$R^3$  represents a  $C_{1-8}$  alkylene group, a 1,2-cycloalkylene group, or a 1,2-arylene group; and

each  $R^4$  independently represents hydrogen or  $C_{1-3}$  alkyl.

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42(New). A method as claimed in claim 41 wherein in formula I:

$R^5$  is hydroxy,  $C_{1-8}$  alkoxy, ethylene glycol, glycerol, amino or  $C_{1-8}$  alkylamido;

$X$  is a bond or a group selected from  $CH_2$ ,  $(CH_2)_2$ ,  $CO$ ,  $CH_2CO$ ,  $CH_2CH_2CO$  or  $CH_2COCH_2$ ;

$Y$  is a bond;

$R^6$  is a mono- or poly(hydroxy or alkoxyated) alkyl group or a group of the formula  $OP(O)(OR^8)R^7$ ; and

$R^7$  is hydroxy or an unsubstituted alkyl or aminoalkyl group.

43(New). A method as claimed in claim 41 wherein in formula I,  $R^3$  is ethylene and each group  $R^1$  represents  $-CH_2COR^5$  in which  $R^5$  is hydroxy.

44(New). A method as claimed in claim 41 in which the compound of formula I is  $N,N'$ -bis-(pyridoxal-5-phosphate)-ethylenediamine- $N,N'$ -diacetic acid (DPDP) or  $N,N'$ -dipyridoxyl-ethylenediamine- $N,N'$ -diacetic acid (PLED).

45(New). A method as claimed in claim 38 wherein said chelate complex is a complex of a linear, branched or macrocyclic chelant selected from polyaminopolycarboxylic acid chelants and carboxylic acid derivatives thereof.

46(New). A method of detecting myocardial ischemia in a human or non-human body, said method comprising administering to said body a physiologically acceptable manganese chelate complex, subjecting said body to a magnetic resonance imaging procedure capable of generating images with time intervals of less than 0.5 seconds and thereafter providing a series of images of the myocardium of said body whereby to identify regions of abnormal blood flow, wherein said complex has a  $K_a$  value of from  $10^7$  to  $10^{25}$  and is a complex of a chelant selected from the group consisting of N,N,N',N",N"-diethylenetriaminepentaacetic acid (DTPA) and 6-carboxymethyl-3,9-bis(methylcarbamoyl-methyl)-3,6,9-triazaundecanedioic acid (DTPA-BMA).

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47(New). A method of evaluating the severity of myocardial ischemia in a human or non-human body, said method comprising administering to said body a physiologically acceptable manganese complex or salt thereof at a dosage of 0.001 to 0.2 mmol/kg bodyweight, subjecting said body to a magnetic resonance imaging procedure as defined in claim 31 and thereafter providing a series of images of the myocardium of said body to indicate the degree of blood perfusion deficit in the myocardium.

48(New). A method of monitoring reperfusion of the myocardium of a human or non-human body, said method comprising administering to said body a physiologically acceptable manganese complex or salt thereof at a dosage of 0.001 to 0.2 mmol/kg bodyweight, subjecting said body to a magnetic resonance imaging procedure as defined in claim 31 and thereafter providing a series of images of the myocardium of said body and identifying regions of reperfusion.

49(New). A method of discriminating between reversibly and irreversibly injured myocardial tissue, said method comprising administering to said body a physiologically acceptable manganese complex or salt thereof at a dosage of 0.001 to 0.2 mmol/kg bodyweight, subjecting said body to a magnetic resonance imaging procedure as defined in claim 31 and thereafter providing a series of images of the myocardium of said body and discriminating reversibly from irreversibly injured tissue.

50(New). A method of distinguishing viable myocardial tissue from necrotic (infarcted) tissue, said method comprising administering to said body a physiologically acceptable manganese complex or salt thereof at a dosage of 0.001 to 0.2 mmol/kg bodyweight, within a period of from 3 to 6 hours following administration of said complex or salt thereof subjecting said body to a magnetic resonance imaging procedure as defined in claim 31 and thereafter providing a series of images of the myocardium of said body and distinguishing viable myocardial tissue from infarcted tissue.